UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

October 29, 2004

MEMORANDUM

Subject: Efficacy Review for EPA File No. 74234-MD-1, LMP-102™
DP Barcode: 301531

From: Tajah L. Blackburn, Ph.D., Microbiologist 10/29/04
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

Thru: Nancy Whyte, Acting Team Leader
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510C)

To: Velma Noble PM 31/ Jacqueline Campbell-McFarlane
Regulatory Management Branch I
Antimicrobials Division (7510C)

Applicant: Intralytix, Inc.
323 W. Camden Street
Baltimore, MD

Formulation from Label

Active Ingredient(s)	% by wt.
Listeria Specific Bacteriophages*.....	0.00001%
Inert Ingredient(s)	99.99999%
Total	100.00000%

*Contains approximately 10^9 PFU/ml

I BACKGROUND

The product, LMP-102™ is a lytic phage cocktail against *Listeria monocytogenes*. LMP-102™ is novel, nonchemical approach for controlling the pathogen, *Listeria monocytogenes*. It is specifically designed for use in food-processing plants and food-handling establishments that have recurrent and hard to manage listeria contamination. LMP-102™ is a pH neutral formulation that is compatible with all types of surfaces. Per the label, LMP-102™ may be used as part of an integrated sanitization/microbial control program with EPA approved sanitizers. The submitted efficacy study was conducted at the University of Maryland School of Medicine, Department of Epidemiology and Preventive Medicine, located at 10 South Pine Street, MSTF Building Room 9-17, Baltimore, MD, 212101, and Intralytix, Inc., 701 E. Pratt Street, Baltimore, MD 21202.

The data package contained a letter from the applicant to the EPA (dated December 29, 2003), EPA form 8570-4, EPA form 8570-34, EPA form 8570-35, copies of modified protocol versions of EPA-approved protocol "Sanitization Study: Quantitative Reduction on a Non-Food Contact Surfaces," two efficacy studies (MRID No. 454535-05 and 461693-04), and the proposed label.

Note– Per Drs. Gary Pasternack and Alexander Sulakvelidze the study entitled "Efficacy of a Bacteriophage Preparation (LMP-102 Against *Listeria monocytogenes* on Non-Food Contact Surfaces" (MRID No. 454535-05), was not submitted in support of registration, but to described the evolution of LMP-102.

II USE DIRECTIONS

LMP-102™ is for use in the control of *Listeria monocytogenes* on non-food contact surfaces in meat, poultry and dairy processing facilities, food-handling establishments and other commercial food-handling facilities. Surfaces that can be treated with LMP-102 include walls, floors, drains, grating and non-food contact equipment. Directions on the proposed label provide the following information regarding the use of the product: Apply LMP-102 to surfaces by spraying or with a cloth or mop. Apply sufficient amounts of LMP-102 so that the target surface is thoroughly covered. About 50 ml of LMP-102 will treat approximately 4½ ft^2 of surface.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Sanitizers (For Non-Food Contact Surfaces)

The effectiveness of sanitizers for non-food contact surfaces must be supported by data that show that the product will substantially reduce the numbers of test bacteria on a treated surface. The test surface(s) should represent the type(s) of surfaces recommended for treatment on the label, i.e., porous and non-porous. Products that are represented as "one-step sanitizers" should be tested with an appropriate organic soil load, such as 5 percent serum. Tests should be performed with each of 3 product samples, representing 3 different

product lots, one of which is at least 60 days old against *Staphylococcus aureus* (ATCC 6538) and either *Klebsiella pneumoniae* (aberrant, ATCC 4352) or *Enterococcus aerogenes* (ATCC 13048 and 15038). Results must show bacterial reduction of at least 99.9 percent over the parallel control within 5 minutes. These Agency standards are presented in DIS/TSS-10.

There are cases where an applicant requests to make claims of effectiveness against additional microorganisms for a product that is to be used as a sanitizer for non-food contact surfaces. The DIS/TSS standards are silent on this matter. Confirmatory test standards would apply. Therefore, 2 product samples, representing 2 different batches, should be tested against each additional microorganism. Results must show a bacterial reduction of at least 99.9 percent over the parallel control within 5 minutes. Furthermore, according to information provided in **Section 12.3.2 of ASTM Method E1153-94, which is a test method for the efficacy of sanitizers for non-food contact surfaces, "an average of at least 7.5 x 10^5 organisms must have survived on the inoculated control squares for the test to be valid."**

In the absence of specific guidance for bacteriophages as sanitizers, DIS/TSS-10 was used as a point of reference, and modified when appropriate. The proposed modifications to DIS/TSS-10 were addressed by the Agency in prior submissions.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID No. 461693-04 "Efficacy, Potency and Stability of LMP-102™ as a Means of Reducing *L. monocytogenes* on Non-Food Contact Surfaces," by Leroy L. Voelker, Ph.D., and Tamar Abuladze. Study conducted at Intralytix, Inc. Study Completion Date– November 3, 2003.

A mixture of the following three *Listeria monocytogenes* strains were used in all experiments (ATCC 13932– serogroup 4b; ATCC 35152– serogroup 1/2a; and *Lm* 301– serogroup 1/2a). Substituting some of the above strains with an alternative *L. monocytogenes* isolate(s) (e.g. ATCC strain 51780 [serotype 1/2b] instead of LM 301, may be utilized. The test culture was established from a transfer from a stock culture, and placed on a MOX plate and incubated overnight at 30°C. A single colony was transferred into LB broth and incubated at 30°C at 150 rpm overnight. On the day of testing, the bacterial culture was poured through a sterile funnel containing sterile cheesecloth to remove any particulates. The amount of culture needed for testing purposes was determined by the OD_{600} for each of three test strains. For *L. monocytogenes*, an OD_{600} in the range of 0.3-0.4 is $\approx$ 1 x 10^9 CFU/ml. By calculating the volume and dilution factor, the concentration of each test strain was adjusted to approximately 1 x 10^7 CFU/ml using LB broth. Each sterile coverslip was inoculated with 0.01 ml of test culture (1 x 10^7 CFU/ml). Three coverslips per batch for all test and control groups were inoculated with test organisms. The number of coverslips inoculated and the number of coverslips used in the assay were documented. The inoculated coverslips were dried in a laminal flow biosafety hood at room temperature for 15 minutes. Post-drying, 0.1 ml of test substance was placed onto the inoculated coverslip, for a contact time of 5 minutes at room temperature. Just prior to the five minute contact time, excess product was drained off the

coverslip. Coverslips were then placed in 50-ml conical tubes containing 20 ml peptone water and vortexed for 0.5 min. The suspension was serially diluted (10^{-1}, 10^{-2}, and 10^{-3}) and filtered immediately through 0.45 µm filter. The filters were washed with 20 ml peptone water. This step is designed to remove most of the unattached phage from the incubation mixture. Testing/validation protocol for residual phage is determined. Note: If the numbers of *L. monocytogenes* recovered from the non-active substance (negative control) are similar to those recovered from neutralizer samples, the filtration step has removed LMP-102 effectively from the incubation mixture after the specified contact time. The filters were subsequently incubated at 30°C overnight. An additional 24-hour incubation at room temperature may be required to better visualize the colonies. Such incubation is deemed acceptable and is recorded in the raw data. The numbers of surviving bacteria present from the filters on the agar plates were quantitated and recorded. The counts were multiplied by the appropriate dilution factor to determine the numbers of organisms surviving treatment of the inoculated coverslip. Controls consisted of sterility, purity, dried organism recovery, and neutralization confirmation.

Note– Per the applicant's enclosure, "This study was not conducted in accordance with the Agency's Good Laboratory Practice (GLP) standards, as specified in 40 CFR § 160. Although the study was not conducted in accordance with GLP standards, the design, performance and study conclusions are scientifically valid and accurate. Consequently, the study should be considered reliable for regulatory decision-making purposes."

Note– The original protocol stipulated that the testing will be performed using three independent batches of LMP-102. Instead, the applicant used five independent batches, to generate more rigorous data pertaining to the efficacy of LMP-102 for reducing the levels of *L. monocytogenes* on non-food contact surfaces.

2. MRID No. 454535-05 "Efficacy of a Bacteriophage Preparation (LMP 102™) Against *Listeria monocytogenes* on Non-Food Contact Surfaces" by Alexander Sulakvelidze, Ph.D. Study conducted at University of Maryland, School of Medicine, Department of Epidemiology and Preventive Medicine. Study conducted date June 2001.

These studies present presumptive/field data pertaining to the efficacy of a bacteriophage preparation (LMP 102) against *Listeria monocytogenes*. This data is being submitted in support of an Experimental Use Permit (EUP) as requested by Intralytix. This study was designed to test whether treatment with a bacteriophage can reduce environmental contamination with *L. monocytogenes*. Plastic surfaces were experimentally contaminated with *L. monocytogenes* (Perdue strains #30, 38, and 47 collectively or individually; Perdue Farms Inc., Salisbury, MD), either as a single strain or as a mixture of three distinct strains. The surfaces were then treated either with an aqueous suspension of polyvalent bacteriophages specific for *L. monocytogenes* or with sterile water. Briefly, the single strain experiment, 5 ml of LB broth was inoculated with a 10 µl loop of *L. monocytogenes* strain #30 and incubated overnight at 30°C. The overnight culture was diluted 1 x 10^5 CFU/ml. Approximately 100 µl of the diluted was spread evenly across the tops of two autoclave plastic boxes (11.5 x 13.5 cm; designated Box A and B single species, Box C and D – multiple species). Boxes were allowed

to dry at room temperature for 2 hours. The top of Box A and C were sprayed with 1 ml of water. The top of Box B and D were sprayed with 1 ml of an aqueous suspension of polyvalent lytic bacteriophages at an infective titer of 1 x 10^5 PFU/ml using a 250-ml spray bottle. Boxes A and B were incubated at room temperature. Swab samples were collected at 3, 5, 24, 48, 72, and 96 hours utilizing a swab moistened with 0.1% peptone broth. The swab sample was eluted into 1 ml sterile 0.1% peptone broth. From the elutant, 0.1 ml broth samples were spread onto a LB agar plate and incubated overnight at 30°C. The following morning the colonies were counted, and titers recorded.

Note– Per the applicant's enclosure, "This study was not conducted in accordance with 40 CFR Part 160. Although the study was not conducted in compliance with the Good Laboratory Practice (GLP) regulations, the design, performance and study conclusions are scientifically valid and accurate. Consequently, the study should be considered reliable for decision-making purposes."

Note– As the result of verbal communications, Intralytix has requested that this Field Test be referenced as background information regarding the evolution of LMP-102, not as efficacy data supporting registration. A letter reflecting this position is forthcoming.

V RESULTS

MRID No. 461693-04

Graphs were submitted to demonstrate efficacy of LMP-102™ in reducing *L. monocytogenes* on non-food contact surfaces (MRID No. 461693-04). The actual data points were not included in the graph. The *n* for each bar was not detailed in the data report. Furthermore, no statistical information was provided in support of the submitted graphs. In the future, data should be presented in tabular form, including the actual data points. Following communications with Intralytix on November 12, 2004, I requested the raw data to support the referenced graphs.

MRID No. 454353-05

Time (Hours)	Box A	Box B	Box C	Box D
0	2.3 x10^3	2.3 x10^3	2.7 x10^3	2.3 x10^3
3	2.0 x 10^3	9 x10^2	2.1 x10^3	4 x10^2
6	1.9 x 10^3	2.3 x10^3	1.8 x10^3	2 x10^2
24	5 x10^2	2 x10^1	3 x10^2	0
48	5 x 10^2	0	4 x10^2	0
72	5 x 10^2	0	4 x10^2	0
96	2 x 10^2	0	2 x10^2	0

Note– This data was not submitted to support registration.

VI CONCLUSION

1. The submitted efficacy studies (MRID No. 461693-04) do not support the use of the cocktail LMP-102™ in the reduction of *L. monocytogenes.* **Full Agency registration cannot be granted until the requested information is received, and acceptance of non-GLP rationale is accepted.** The following two items, concerning non-GLP rationale and bacterium inoculum discrepancies, with appropriate comments are detailed below:

(A) Per the letter emailed from Eliot Harrison, justification for submission of non-GLP study has been provided to the Agency. According to the submitted letter, the applicant position is that "even though the study was not certified as GLP compliant, we believe the study is valid and reproducible particularly since many of the key GLP elements, as noted below, were followed," (excerpts from the letter in bold-faced type):

- **The study director, Roy Voelker, is a Ph.D., microbiologist with extensive relevant training, education and experience. All technical personnel engaged in the conduct of study also have extensive relevant training, education and experience.**

Agency's Response: A list of all technical personnel should be submitted in support of the registration, and to support the applicant's non-GLP position.

- **The test system was as specified in the protocol and all raw experimental data, including observations of unanticipated responses, were accurately recorded.**

Agency's Response: Information provided as stated.

- **The test substance was properly identified with the appropriate lot number, and its production traceable at each stage. It was appropriately tested for identity, potency, and purity.**

Agency's Response: Information provided as stated.

- **The test culture (mixture of three *Listeria monocytogenes* strains) was prepared from a fully documented master bank of specified *Listeria monocytogenes* strains that were fully and appropriately tested for identity, potency and purity.**

Agency's Response: Information provided as stated. A growth curve should be submitted to support the OD values, since there are discrepancies in the expected versus actual CFU/ml counts.

– **The protocol was reviewed and approved by EPA prior to initiating the study. All relevant positive and negative controls were included and the study protocol was followed to the letter.**

Agency's Response: Information provided as stated.

– **The raw data was rigorously analyzed and the results were robust.**

Agency's Response: Request for raw data from the submitted graphs was made on November 12, 2004. This information is forthcoming.

In addition to the Agency's responses as outlined above, the following guidelines under GLP were not addressed in the submitted study:

(1) The exact dates of study initiation, study completion, experimental start and experimental termination are not provided. A range of study dates (between October and December 2003) is listed on page 5 of 27 in the submitted report. However, exact dates for each phase must be provided. Definitions are provided below:

(a) **Experimental start date**. Defined as the first date the test substance is applied to the test system.
(b) **Experimental termination date**. Defined as the last date on which data are collected directly from the study.
(c) **Study completion date**. Defined as the date that the final report is signed by the study director;
(d) **Study initiation date**. Defined as the date the protocol is signed by the study director;

(2) The statistical methods employed for analyzing data [40 CFR §160.185(j)(3)];

(3) The signed and dated reports of each of the individual scientist or other professional involved in the study, including each person who at the request or direction of the testing facility or sponsor, conducted an analysis of evaluation of data or specimens from the study after data generation was completed [40 CFR §160.185 (j)(12)]. Signatures were omitted from page 5 of 27 of the submitted efficacy study (MRID No. 461693-04);

(4) The statement prepared and signed by the quality assurance unit [40 CFR §160.185 (j)(14)];

(5) The final report should be signed and dated by the study director [40 CFR §160.185 (j)(14)(b)];

(B) The bacteria inoculum, as stated in MRID 461693-04, is unclear;

The study protocol requires an inoculum 0.01 ml of the test culture (1 x10^7 CFU/ml) onto each sterile coverslip using an appropriate micropipette. (Cited from Test surface/Coverslip Inoculation section, page 12 of 27). However, on page 19 of 27, (Section 3.2.1– Efficacy of

LMP-102 on Non-Food Contact Surfaces) the applicant states that **"the initial protocol called for the plating 10^{-1}, 10^{-2}, and 10^{-3} dilutions for negative control, positive control and neutralizer groups. This was based on the assumption that 100% (1 x 10^7 CFU) of the *Listeria* applied to the glass coverslips would be recovered. Based on several experiments, the typical recovery is 1 x 10^3 to 1x10^4 CFU. Thus, the 10^{-1} and 10^{-2} dilutions are the most appropriate and statistically significant dilutions to use for counting from these three groups– and we used these two dilutions during our studies."** Based on the applicant's statement, the 0.01 ml inoculum of the test culture onto the sterile coverslip is significantly less (on the order of 1 x 10^3 to 1 x 10^5 CFU/ml following dilution) than the initial expected starting value of 1 x10^7 CFU/ml.
Follow-up: Per the conference call on November 12, 2004, I was informed by Alexander Sulakvelidze, Ph.D., that the actual inoculum count ranged from 1 x 10^3 to 1x 10^5 CFU/ml. This range is quite large and highly variable. In the cases were the inoculum borders on 1x 10^3 CFU/ml, demonstrating a 3-log reduction is highly questionable.

VII COMMENTS RELATED TO SUBMITTED PROTOCOL AND DATA

Study Entitled: Efficacy, Potency and Stability of LMP-102 as a means of Reducing *L. monocytogenes* on Non-Food Contact Surfaces (MRID No. 461693-04)

Applicant's Statement: The LMP-102 preparation is stable for 1 year when kept refrigerated (2-6°C) in dark. When used as prescribed, LMP-102 is effective in reducing by ≥ 3 logs, contamination of non-food contact surfaces with *L. monocytogenes* in 5 minutes of contact time. (Cited from Summary, page 7 of 27)
Agency's Response: The proposed label does not reflect a 1 year expiration date. The proposed label does recommend storage at 4°C. However, there is no statement that indicates that the product should be kept in the dark.

Applicant's Statement: 1. Just prior to the five minute contact time, remove (using alcohol flamed and cooled forceps) the coverslip from the petri dish and drain off any excess product. 2. Place the cover slips into 50-ml conical tubes containing 20 ml peptone water. Vortex gently. (Cited from Subculture of Treated Coverslips, page 12 of 27)
Agency's Response: The statement "just prior to five minutes" is quantitatively ambiguous.
Agency's Response: Do steps 1 and 2 as detailed in the protocol (and included above), exceed the 5 minute contact. The exact time of contact time is questionable.

Applicant's Statement: "The protocol called for the plating 10^{-1}, 10^{-2}, and 10^{-3} dilutions for negative control, positive control and neutralizer groups. This was based on the assumption that 100% (1 x 10^7 CFU) of the *Listeria* applied to the glass coverslips would be recovered. Based on several experiments the typical recovery is 1 x 10^3 to 1x10^4 CFU/ml. Thus, the 10^{-1} and 10^{-2} dilutions are the most appropriate and statistically significant dilutions to use for

counting from these three groups– and we used these two dilutions during our studies." (Cited from 3.2.1 Efficacy of LMP-102 on Non-Food Contact Surfaces, page 19 of 27)
Agency's Response: Based on the actual number of CFU/ml, it appears that the starting counts are 1 x 10^5 CFU. A growth curve should have been included in the study to substantiate the OD values submitted. However, actual plate recovery is preferred.

Applicant's Statement: "As noted in the Introduction, many disinfectants are ineffective/have reduced effectiveness when the test organisms are dried onto the environmental surfaces– conditions likely to be encountered in real-life food processing facility. Thus, in order to more accurately mimic the real-life conditions under which LMP-102 is to be used, we used 5% skim milk to 'dirty' the glass cover slips prior to contamination with *L. monocytogenes* and application of LMP-102. Briefly, 0.01 ml of 5% skim milk solution was applied per coverslip, and was allowed to dry (in a laminar flow biosafety hood) at room temperature for 5-10 minutes (or until completely dry). Subsequent testing was performed exactly as described in the protocol. (Cited from 3.2.1 Efficacy of LMP-102 on Non-Food Contact Surfaces, page 19 of 27)
Agency's Response: Was this soil approved by the Agency in prior submissions?

Applicant's Statement: Each lot of LMP-102 produced must show a statistically significant reduction of *L. monocytogenes* counts compared to the non-active control counts to be considered efficacious. Results will be reported as log reductions where reduction of 99% and 99.9% are equal to a 2 and 3 log reductions respectively. (Cited from 3.3.1 Efficacy of LMP-102 on Non-Food Contact surfaces, page 20 of 27).
Agency's Response: (1) Utilizing the OD values, expected plate counts, and actual plate counts, it appears that there is a significant difference in counts, on the order of 10^2 CFU/ml. Based on the differences in plate counts, a 3-log reduction cannot be demonstrated with the amount inoculated on the slide and the final dried recovery counts. (2) What statistical tests were performed?

Applicant's Statement: Three manufacturing lots of LMP-102 were stored at 4°C for different lengths of time up to 405 days. The stability of these lots was evaluated by determining their potency according to the protocol described. (Cited from 3.2.3. and 3.3.3 LMP-102 Stability, page of 27). LMP-102 will be considered stable for all lots that have been stored at 4°C and continue to pass the potency test.
Response: Considering the inevitability of phage resistance, has the applicant determined when this may occur with LMP-102? Furthermore, when is it determined that the phage cocktail be reformulated as the result of acquired resistance?
Follow-up: Per the conference call on November 15, 2004, Alexander Sulakvelidze, Ph.D., stated that appropriate "checks and balances" are in place to determine the continued efficacy LMP-102 in multiple environments. Furthermore upon determination of acquired resistance, LMP-102 will be reformulated, and necessary efficacy data will be resubmitted.

Applicant's Statement: Incubate all tubes overnight (16± 1 hours) at 30°C±2°C without shaking (Cited from Appendices, page 27 of 27).
Response: Protocols requiring the use of a spectrophotometer often require a vortexing or

agitation step to re-suspend the particulates that have settled at the bottom of the cuvette or test tube. Following an incubation of 16 hours, to omit shaking, vortexing or agitation is unorthodox.
Follow-up: During the conference call on November 12, 2004, Alexander Sulakvelidze, Ph.D., assured me that this technique for the determination of bacteriophage potency was cited from a reputable publication. The reference, with rationale, is forthcoming.

Applicant's Statement: Manufactured lots of LMP-102 will be considered potent if the OD_{600} of the test sample is $\leq$ 0.06, not potent if the OD_{600} is $\geq$ 1 and to have some residual potency if the OD_{600} is in the range of 0.06-0.1 against all three L. monocytogenes strains, The OD_{600} for all control replicates and the negative control strain (ATCC 47014) must be $\geq$ 0.15 for the assay to be considered valid. (Cited from 3.3.2 LMP-102 Potency, page of 20 of 27)
Response: It appears as though there is a typo in the not potent range. Considering the residual potency cited at 0.06-0.1, should the non-potent be 0.1 instead of 1?

Study Entitled: Efficacy of a Bacteriophage Preparation (LMP-102) Against *Listeria monocytogenes* on Non-Food Contact Surfaces (MRID No. 454535-05)

Note– This study was submitted for background information only, and is not in support of current registration (per Drs. Pasternack and Sulakvelidze).

Test Results from (Single Strain Experiment)

MRID No.	Time post exposure to phage (h)	Maximum theoretical log reduction	Observed log reduction
454535-05	3	3.36	0.35
	6	3.30	0.80
	24	3.28	1.40
	48	2.70	2.70 (sterile)
	72	2.70	2.70 (sterile)
	96	2.30	2.30 (sterile)

Test Results (Multiple Strain Experiment)

MRID No.	Time post exposure to phage (h)	Maximum theoretical log reduction	Observed log reduction
454535-05	3	3.32	0.48
	6	3.26	0.95
	24	2.48	2.48 (sterile)
	48	2.60	2.60 (sterile)
	72	2.60	2.60 (sterile)
	96	2.30	2.30 (sterile)

1. Per the submitted Test Results Chart on page 6 of the field study (included above), it appears that a 3-log reduction is observed only after a 48-hour contact time. The proposed label and laboratory results demonstrate efficacy at 5-minute contact time.
How do these contact times (3, 6, 24, 48, 72, and 96 hours) relate to the laboratory study and the proposed label?
Response from Intralytix: Study not in support of registration.

2. When is the neutralization step in the field test?
Response from Intralytix: No neutralization for this test.

Additional Questions posed to Intralytix

Question: The first step of bacteriophage infection is adsorption, or the attachment of the virus to the bacterial surface. Adsorption has two primary stages, a reversible stage and an irreversible stage. In the reversible stage the tail fibers at the tip of the tail attach to the bacterial surface. Bacteriophages attach to specific outer membrane proteins, which surrounds the rigid peptidoglycan layer of the bacterial cell wall. There may also be other bacteriophage receptors that facilitate the process of attaching to the bacterial cell. Phage attachment is reversible until the second stage of adsorption, in which the short tail fibers attach and the phage becomes permanently attached. **What is the timeline of the bacteriophage attachment process, as it relates to the specified contact time on the proposed label?**
Response from Intralytix: A time period of 20-40 seconds is needed for irreversible attachment to occur; this is well within the 5 minute contact time.

Question: The listed contact times for the laboratory study and field study are inconsistent. What is the effective contact time for LMP-102?
Response from Intralytix: Per the laboratory studies, the contact time is five minutes. The Field Test should not be referenced in support of product registration.

Question: What type of Quality Assurance program is utilized to test and address bacteriophage acquired resistance?
Response from Intralytix: Measures are currently in place to address resistant bacteriophages. These measures were not detailed.

Question: On the proposed label, the storage condition is 4°C, no expiration date is listed. In the Summary section (page 7 of 27) of the efficacy report, the stability of LMP-102 is "1 year when kept refrigerated (2-6°C) in dark." Should the label list "in dark" as a storage condition? Does light mitigate the efficacy of LMP-102?

VIII RECOMMENDATIONS

1. On the proposed label, the contact time should be listed under Directions for Use section. Currently, it is listed in the Product Description section.

2. On the proposed label, an expiration date should be listed, considering the possible mitigating effects of light, and extended exposure to higher temperatures during use.